# THE TOTAL NON-PROTEIN NITROGEN OF THE BLOOD IN PREGNANCY AND ECLAMPSIA.[1]

By Clifford B. Farr, A.M., M.D.,

AND

Philip F. Williams, M.D.,

PHILADELPHIA.

(From the John Herr Musser Department of Research Medicine, University of Pennsylvania, and the Obstetrical Service of the Hospital of the University of Pennsylvania.)

In the course of some recent work on the non-protein nitrogen ("rest" nitrogen) content of the blood in nephritis,[2] we had the opportunity to examine specimens from a number of patients suffering from eclampsia. As the results obtained in these few cases seemed to promise information of value, we collected additional material, and now present our findings in some twenty pregnant women, one-third of whom were normal while the remainder presented toxic phenomena of one sort or another. For the determination of the total non-protein nitrogen and urea of the blood we employed the technique recently perfected by Folin.[3] Only 5 or at the most 10 c.c. of blood are required, an amount readily obtained from a vein by a syringe. Strauss[4] has recently combined the method of collection and precipitation of the blood devised by Folin, with the ordinary Kjeldahl determination of the nitrogen, which may possibly be a fairly staisfactory procedure for the detection of gross variations when the special apparatus for the Folin method is not available. So far as we can ascertain no one has yet published a series of cases by the improved method we have employed, nor are data of any sort with reference to the nitrogen or urea of the blood in pregnancy available in any quantity.

Landsberg[5] examined the oxalated blood-plasma in a series of 18 pregnant women, clinically normal, and found, by the Kjeldahl method, the average content of "rest" nitrogen to be 24 mg. per 100 c.c. In 10 parturients the average was 23 mg., while in 8 normal non-pregnant women the average was 21 mg. per 100 c.c. In 1 case, however, in which the pregnancy was complicated by edema, albuminuria, and cylindruria the blood-plasma obtained ten days before delivery showed a content of 276 mg., a very considerable increase over normal.

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[1] Read before the Pathological Society of Philadelphia, October 9, 1913.

[2] C. B. Farr, and J. H. Austin, The Total Non-protein Nitrogen of the Blood in Nephritis and Allied Conditions, Jour. Exper. Med., 1913, xviii, 228.

[3] Newer Methods for the Determination of Total Non-protein Nitrogen, Urea, and Ammonia in the Blood, Jour. Biol. Chem., 1912, ii, 527.

[4] Zur Prognosenstellung bei Nephritis, Zeitsch. f. Urol., 1913, vii, 287.

[5] Utersuchungen ueber den Gehalt des Blutplasmas an Gesamteiweiss, Fibrinogen und Reststickstoff bei Schwangeren, Archiv. f. Gynak, 1910, lcii, 693.

Zangemeister[6] bases his figures on the 9 cases of eclampsia which he examined by a similar method, and found them to range between 15.7 and 44.3 mg., with an average of 25.8 mg. per 100 c.c. He determined the freezing-point of the plasma and reached the conclusion that, "As a rule 'rest' nitrogen is somewhat increased in eclampsia dependent upon the molecular concentration of the blood. There are single cases, however, in which this increase fails, even although the cases may have further convulsions. This increase should not be considered as a cause of eclampsia, but rather a secondary appearance, due to a lowered diuresis." In this connection it may be stated that Strauss has found no definite relation between the nitrogen content and the depression of the freezing-point.

Herter[7] in an article which does not give his actual figures or methods, states that in his study of the blood in six cases of eclampsia there was no increase in the percentage of urea. In a subsequent paper he[8] concluded that in cases of eclampsia without chronic nephritis the percentage of urea in the blood was almost regularly normal or only slightly increased in amount. When chronic nephritis existed the urea was apt to be high, and when this was the case a fatal outcome was to be expected.

In the following table we have classed our cases in four groups. Group A includes seven cases of normal pregnancy. The total non-protein nitrogen ranged from 21 to 31 mg. per 100 c.c., while the urea (or more precisely the ammonia-urea fraction) varied from 7 to 15 mg. per 100 c.c. of whole blood. These figures we consider perfectly normal, and this is confirmed by the other tabulated data, with the exception, perhaps, of the phenolsulphonephthalein test, to which we will refer subsequently.

Group B consists of three cases, in which the most prominent symptoms were referable to renal insufficiency; in one case valvular cardiac disease was added as a complicating factor. In each of these cases the pregnancy was interrupted on account of the increasing severity of the symptoms. In these cases the total non-protein nitrogen ranged from 34 to 52 mg. per 100 c.c. and the ammonia-urea fraction from 11 to 30 mg. per 100 c.c. of whole blood. The estimatioms were repeated in 2 of these cases during the puerperium; in 1 case a slight and in 1 case a considerable decrease was found. It will also be noticed that the decrease was practically all in the urea. In 1 case the history suggested chronic nephritis, and the urine contained albumin and casts when the patient left the hospital.

[6] Untersuchungen ueber die Blutbeschaffenheit und die Harnsecretion bei Eklampsie, Zeitsch. f. Geburtsch. u. Gynak., 1903, i, 385.

[7] The Pathology of Uremic Intoxications, Montreal Med. Jour., 1898, xxvii, 321.

[8] C. A. Herter, On Urea in some of Its Physiological and Pathological Relations, Johns Hopkins Hospital Reports, 1900, ix, 69.

### GROUP A—CASES CLINICALLY NORMAL.

| No. | Age | Para | Month of preg. | Nitrogen, mg. per 100 c.c. | Urea, mg. per 100 c.c | Phthalein 1st hour | Phthalein 2d hour | Phthalein total | Blood pressure | Edema | Albumin | Casts |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 22 | II | 5th | 20 | 6 | .. | .. | .. | 120 | none | none | none |
| 2 | 27 | II | 9th | 23 | 10 | 21 | 11 | 32 | 140 | none | none | none |
| 3 | 21 | I | 9th | 25 | 8 | 25 | 3 | 38 | 125 | none | trace | none |
| 4 | 25 | I | 7th | 27 | 14 | .. | .. | .. | 125 | none | none | none |
| 5 | 27 | IV | 7th | 30 | 13 | .. | .. | .. | 130 | slight | trace | none |
| 6 | 16 | I | 9th | 28 | 14 | 25 | 25 | 50 | 130 | none | trace | none |
| 7 | 19 | I | 8th | 27 | 10 | 28 | 19 | 47 | 140 | none | none | none |

### GROUP B—CASES WITH RENAL SYMPTOMS PREDOMINATING.

| No. | Age | Para | Month of preg. | Nitrogen, mg. per 100 c.c. | Urea, mg. per 100 c.c | Phthalein 1st hour | Phthalein 2d hour | Phthalein total | Blood pressure | Edema | Albumin | Casts |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 37 | I | 5th | 33 | 16 | 15 | 9 | 24 | 175 | Extreme | Heavy cloud | Hyaline granular |
| 1 | 37 | I | 10 days after delivery | 29 | .. | .. | .. | .. | 160 | Slight | Trace | Occasionally |
| 2 | 39 | II | 9th | 52 | 30 | 20 | 15 | 35 | 204 | Moderate | Light cloud | Hyaline granular |
| 2 | 39 | II | 14 days after delivery | 29 | 7 | 23 | 12 | 35 | 195 | None | Trace | None |
| 3 | 20 | I | 9th | 35 | 11 | 19 | 15 | 34 | 165 | Moderate | Heavy cloud | None |

### GROUP C—CASES WITH ECLAMPTIC CONVULSIONS.

| No. | Age | Para | Month of preg. | Nitrogen, mg. per 100 c.c. | Urea, mg. per 100 c.c. | Phthalein 1st hour | Phthalein 2d hour | Phthalein total | Blood pressure | Edema | Albumin | Casts | Notes |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 18 | I | 1 day post partum | 25 | 11 | 32 | 20 | 52 | 160 | none | Trace | None | |
| 2 | 24 | II | 8th | 37 | 25 | .. | .. | 20 | 195 | Marked | Heavy cloud | Hyaline granular | Died |
| 3 | 29 | III | 9th | 40 | 27 | 0 | 0 | 0 | 210 | Slight | Heavy cloud | Hyaline granular | Died |
| 4 | 23 | I | 1 day post partum | 46 | 30 | 35 | 20 | 55 | 162 | Slight | Heavy cloud | Hyaline granular | |
| 4 | 23 | I | 14 days post partum | 35 | 14 | .. | .. | .. | 140 | None | Trace | None | |
| 5 | 19 | I | 9th | 54 | .. | 20 | 3 | 23 | 165 | Marked | Boiled solid | Granular | |
| 5 | 19 | I | 11 days post partum | 25 | 11 | 25 | 20 | 45 | 140 | None | Light cloud | None | |
| 6 | 30 | I | 7th | 51 | 22 | 20 | 18 | 38 | 210 | Slight | Light cloud | Granular | |
| 7 | 29 | I | 6th | 72 | 50 | .. | .. | .. | 180 | Marked | Light cloud | Granular | Died |

GROUP D.

| No. | Age | Para | Month of preg. | Nitrogen, mg. per 100 c.c. | Urea, mg. per 100 c.c. | Phthalein |  |  | Blood pressure | Edema | Albumin | Casts | Notes |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|  |  |  |  |  |  | 1st hour | 2d hour | total |  |  |  |  |  |
| 1 | 24 | II | 3d | 22 | 8 | 50 | 18 | 68 | 116 | Slight | None | None | Salivated |
| 2 | 32 | II | 8th | 23 | 11 | .. | .. | .. | 160 | Slight | None | None | Headache<br>Retinitis |
| 3 | 20 | III | 8th | 20 | 8 | 30 | 10 | 40 | 130 | None | None | None | Chorea |

Group C includes seven cases presenting convulsions as a prominent clinical symptom. The eclamptic seizures varied in number and severity. One case, the first in this group, after a normal delivery had a typical eclamptic convulsions further attacks were avoided by immediate treatment. In this instance the total non-protein nitrogen was within normal limits, 26 mg. In the other cases the figures ranged from 38 to 72 mg.; both patients represented by these extremes died, but several showing intermediate values recovered. Of the latter two were examined again after they had made clinical recoveries, and in each a considerable reduction in the nitrogen was found.

It will be noted that the other laboratory findings were in the most part confirmatory.

Group D comprises three dissimilar cases: one of uncontrollable vomiting during the third month of pregnancy; one of persistent headache, hemorrhagic retinitis, and high blood-pressure, without urinary changes; and one in which the pregnancy was interrupted at the eighth month on account of a chorea of increasing severity. In none of these cases was there any increase either in the nitrogen or in the urea, the former ranging from 21 to 24 mg. per 100 c.c. and the latter from 8 to 12 mg. per 100 c.c. of whole blood. In the first case the vomiting ceased after admission to the hospital, but marked salivation persisted for some time. In the second case the symptoms improved after rest in bed, and practically disappeared after delivery. In the third case the outcome was also satisfactory.

In 15 out of the 20 cases the functional efficiency of the kidneys was estimated by the phthalein test of Rowntree and Geraghty. In general there was a tendency to slightly subnormal values even in normal cases; in the pathological cases there was usually a correspondence between the nitrogen retention and the diminished phthalein excretion. In one case, however, the nitrogen fell rapidly, with clinical improvement, but there was no rise in the phthalein elimination. The amount of non-protein nitrogen retained is probably an index of the temporary degree of toxemia (uremia literally), while the phthalein elimination is an index of the excretory efficiency of the kidneys. In our normal cases the two-hour elimination ranged from 32 to 50 per cent.; in the cases with renal symptoms, in Group B from 24 to 35 per cent.; and in the eclamptics from 0 to 52 per cent. In the last group the figures were far from consonant with the clinical symptoms—that is, if we suppose the latter to be due in any way to renal inadequacy.

Turning to the literature we find that Sondern and Harvey[9] in a series of 18 pregnant women, clinically normal, determined an excretion of phthalein of from 21 to 58 per cent. in two hours, with an average of 45 per cent.; 1 case with a true renal lesion having convulsions, eliminated 24 per cent; 1 case in which albumin and casts disappeared from the urine shortly after delivery eliminated 38 per cent. Goldsborough and Ainley in normal pregnant[10] women found the excretion to vary between 13 and 67 per cent, with an average of 47 per cent. In the puerperium the figures ranged from 48 to 76 per cent., with an average of 61 per cent. Both averages are below that of healthy non-pregnant individuals. Erne[11] in two normal pregnant women found 70 and 72 per cent. of the phthalein eliminated; in a case of eclampsia at the fourth month of pregnancy, two tests showed 62 and 70 per cent. respectively. A case of renal disease in a pregnant woman showed 42 and 44 per cent. on two examinations.

The blood-pressure in Groups B and C showed a definite increase above the normal in all cases; in no case was the systolic pressure less than 160 during the acute stage. In the remaining normal and miscellaneous cases the blood-pressure was 140 or less in all, with one exception already noted. The urinary changes were also strictly consistent with the clinical symptoms.

Conclusion. In normal pregnant women the total non-protein nitrogen does not usually exceed 30 mg. per 100 c.c. of whole blood. In general hospital cases without demonstrable renal lesions it may frequently reach 40 mg. or more. Slighter disturbances of function are therefore more clearly defined in the former class.

In all cases of pregnancy in which there was definite renal insufficiency or eclampsia, with one exception, there was always a slight and in most cases a considerable increase in the total non-protein nitrogen. The degree of retention was similar to that found in parenchymatous nephritis rather than the higher grade common in the interstitial variety. It bore no definite relation to the severity of the symptoms. In only one case did the figures reach a height which, according to Strauss,[12] would suggest a dubious prognosis. This patient died; another, with much less retention, also died.

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[9] The Phenolsulphonephthalein Test for Estimating Renal Function in Pregnancy, Bulletin of New York Lying-in Hospital, 1012, viii, 172.

[10] The Renal Activity in Pregnant and Puerperal Women as Revealed by the Phenosulphonephthalein Test, Jour. Amer. Med. Assoc., 1910, lv, 2058.

[11] Functionelle Nierenprufung mittels Phenolsulphonephthalein nach Rowntree und Geraghty, Münch. med. Woch., 1913, lx, 510.

The relatively normal elimination of phthalein in some cases of eclampsia and the markedly lowered excretion in some clinically normal cases will not permit us to draw any conclusions as to its real diagnostic or prognostic value from this brief series.

The presence of a rising blood-pressure, the condition of the urine as regards albumin and casts, and the clinical picture are severally more important than either of the newer methods we have employed. Further experience may modify this view, for Widal considers the examination of the blood of greater prognostic, if not diagnostic, value than the examination of the urine.

We are indebted to Dr. R. C. Norris for the privilege of studying in this connection several interesting cases at the Preston Retreat.

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# PROLAPSE OF THE OVARY: ITS RATIONAL MANAGEMENT.

By Chauncey D. Palmer, M.D.,
EMERITUS PROFESSOR OF OBSTETRICS AND GYNECOLOGY IN THE MEDICAL DEPARTMENT OF CINCINNATI UNIVERSITY.

Any prolapse of the ovary, as a distinct, clearly defined, and well-recognized entity, is a morbid condition of a not uncommon occurrence. That this organ of the female sexual system can be so displaced must be apparent to all observing gynecologists.

The left ovary, experience teaches us, is more frequently so disordered. Thus, firmly connected with the uterus by the short, stout, fibrous ovario-uterine ligament, it must, by forces of necessity, in the normal movements of the body, be altered somewhat in its position in various directions; and situated normally on the posterior and upper surfaces of the broad ligament, it is also put in intimate association with the physiological position and condition of the rectum, namely: its distentions as a reservoir for fecal matter and a channel for its evacuation. The physiological movements of the human body in daily life necessarily imply many alterations in the posture of the pelvic viscera to a varying degree. The wise dispensation of nature that an ovary can materially change its position without any derangement of its sensation or function is one of the many provisions of our created organization.

A displacement of any of the internal genitalia of the human female is then a morbid entity only when these alterations in position are persistent and unalterable by natural efforts, and when

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[12] Loc. cit.